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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,310	07/25/2003	Cydney C. Brooks	ADY-009	1899

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EXAMINER

MITRA, RITA

ART UNIT PAPER NUMBER

1653

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/627,310

Applicant(s)

BROOKS, CYDNEY C.

Examiner

Rita Mitra

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-12 and 27-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-12, 27-31, 45 and 46 is/are rejected.
- 7) ☒ Claim(s) 9-12 and 27-46 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/22/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Applicant's Amendment and Reply in response to office action dated November 4, 2005, filed on May 3, 2006 is acknowledged. Claims 1-8 and 13-26 have been cancelled. New claims 27-46 have been added. Therefore, claims 9-12 and 27-46 are currently under examination.

Response to Amendments and Remarks

Objection/Rejection

The objection to the Abstract is withdrawn in view of amendment to the abstract.

The objection to the specification is withdrawn in view of providing the Sequence identifier to the embedded sequences is withdrawn in view of amendment to the abstract.

Rejections - 35 USC § 112, Second Paragraph

Rejection of claims 9-12 are withdrawn in view of fully spelled out abbreviation "FHOS."

Rejection of claim 12 is withdrawn in view of withdrawing the term "portion" from the claim.

Objection to the Claims

Claims 9-12 and 27-46 remain/are objected to because the claims describe a sequence that is set forth in the "Sequence Listing" and embedded in the text of the specification, however no reference is made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" See 37 C.F.R. § 1.181(d). This objection may be overcome by providing sequence identifier to the claims. In response Applicants submit that the specification has been amended to specify that the nucleotide and amino acid sequences of human FHOS are the sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 2 respectively, thus a reference to sequence identifiers should not be required in the claims. Applicants' arguments are not persuasive because although the

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claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26USPQ2d 1057 (Fed. Cir. 1993).

New Ground of Rejection

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 29, 45 and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a method of identify a compound suitable for use in treating diabetes or insulin resistance in a subject, said method comprising contacting a cell capable of expressing FHOS mRNA with a test compound and determining the effect of the test compound on expression of FHOS mRNA, does not reasonably provide enablement for any fragments of FHOS protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard the factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The factors include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 12, 29, 45 and 46 drawn to a method of identify a compound suitable for use in treating diabetes or insulin resistance in a subject, said method comprising contacting a FHOS or biologically active fragment thereof with a test compound and determining the effect of the test compound on a biological activity of the FHOS protein or biologically active fragment thereof,

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wherein a stimulatory effect is indicative of the compound being suitable for use in treating diabetes or insulin resistance in said subject.

The specification describes a FHOS polypeptide, which comprises or consists of amino acid sequence of SEQ ID NO: 2 or is encoded by a polynucleotide comprising or consisting of the sequence of SEQ ID NO: 1 (see page 2, lines 30-32, Figure 3A-B and 3C).

The specification, however, only discloses cursory conclusions, without data to support the findings that the use of fragments of FHOS in the claimed screening method of compounds. The specification indicates in the paragraph bridging page 3 and page 4 that the "FHOS protein" refers to any form of FHOS polypeptide, for example full-length polypeptides and FHOS fragments (e.g. bioactive fragments, structural and/or functional domains, and the like). The term "FHOS nucleic acid molecule" refers to any form of FHOS polynucleotide, for example polynucleotides encoding full-length FHOS proteins, polynucleotides encoding FHOS fragments (e.g. bioactive fragments, structural and/or functional domains, and the like). However, the specification fails to describe screening any compound that comprises steps of providing fragments of FHOS.

Furthermore, the specification discloses therapeutic methods such as gene therapy (page 6), protein therapy (page 13) using FHOS proteins and fragments thereof. However the specification fails to provide any structure and function of these fragments, or the positions in relation to the FHOS protein or nucleic acid sequences. The specification fails to describe any such fragments that retain the activity of the wild type FHOS protein, which can replace or supplement the full length FHOS protein.

In the instant case, the amount of experimentation is enormous since the number of changes from the specific sequence are large. Therefore, it is necessary to perform further experimentation to determine the biological properties of these fragments. Without such guidance, the experimentation left to those skilled in the art is undue. One of skill in the art would have to make and test each one to determine if it had the FHOS activity of the parent protein. The amount of guidance presented is limited to the exact sequence. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled.

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The prior art has identified and characterized the FHOS full-length protein (see Westendorf et al., Gene, Vol. 232, pp 173-182, 1999), however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the structure and function of various FHOS molecules enabling for fragments. Moreover the prior art does not disclose an assay for determining the FHOS activity of the fragments.

The breadth of the claims is broad and encompasses an unspecified number of variants regarding the FHOS peptide products as biological active fragments, which are not specifically described or demonstrated in the specification. The specification provides a generic description at pages 13-14 how to make these fragments, however the specification does not describe or demonstrate the use of FHOS or functional fragments thereof for identifying compounds suitable for use in treating diabetes or insulin resistance in a subject that is encompassed by present invention. However, neither the peptide fragments of FHOS demonstrate any activity of FHOS nor they are used for identifying compounds that is used in treating diabetes or insulin resistance.

Claims 45 and 46 require a functional fragment of FHOS that is capable of binding to FHOS target molecule. However, the disclosure fails to provide a description of a fragment that demonstrates such activity. Therefore as the specification fails to describe adequately the structure and function of those fragments, one skilled in the art would not recognize a specific utility for the fragments and would not know how to use them. Thus, for the reasons set forth above, undue experimentation is required to make and use the claimed FHOS fragments. Thus, further experimentation is required to make and use the claimed invention.

In the instant case, the amount of experimentation is enormous since the number of changes from the specific sequence are large, one of skill in the art would have to make and test each one to determine if it had the FHOS activity of the parent protein. The amount of guidance presented is limited to the exact sequence. No discussion is present as to where the changes might be made to the sequence. The art is unpredictable. The effect of one or a few conservative substitutions might be somewhat predictable, if the active areas of the molecule were known, but more changes than that, are less predictable. The effect on function of this many changes is clearly unpredictable. There is no working examples that demonstrate the claimed variants.

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Finally, these claims are very broad in the sense that many different FHOS protein fragments and fall within the scope of the claims.

Based on this analysis, the finding of undue experimentation is mandated.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

“The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.”

Claim 12 remains/is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite because of the use of the term “fragment.” It is not clear what is the size of the fragment and the position in relation to the amino acid sequence of full length FHOS protein. It is also not clear whether the fragment is from N-terminal or C-terminal amino acid sequence of FHOS.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-12, 27, 28, 29, 30, 31 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by Tojo et al. (US 2004/0072742 A1, published April 15, 2004, priority date December 20, 1999). The reference teaches a protein or a partial peptide and DNA encoding the same are useful as preventives/remedies for diseases. Tojo et al. also teaches a method of screening a compound that inhibits the binding of said protein and partial peptide to insulin responsive aminopeptidase (IRAP) or to glucose transporter 4 (GLUT4), wherein said compound

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is used as a preventive /remedy for diseases, e.g., hyperglycemia, diabetes mellitus (see abstract, paragraph 0031 at page 2, 0037 at page 3, 0197 at page 13, 0207 at page 14, 0221, 0224 at page 16, 0492 at page 33), wherein the test compounds are selected from peptides, proteins, non-peptide compounds, synthetic compounds, fermentation products, cell extracts, vegetable extract, animal tissue extracts and blood plasma (see 0226 at page 16, Examples 2, 9, 0493 at page 33). Tojo's protein II includes a human spleen derived protein containing the amino acid sequence of SEQ ID NO : 2, that is highly homologous (substitution of 9 amino acids in the total 1164 amino acids, that is 99.2% sequence identity) to FHOS protein described by Westendorf et al. (Gene, 232, 173-182, 1999, Genbank Accession NO AF113615). See Figures 6-11, 16, 0085 at page 5, SEQ ID NOs: 2 and 4, Examples 2, 9. Tojo's protein is having the structure of the claimed FHOS protein of instant application considered anticipating the binding of the claimed protein to IRAP or GLUT 4 (claims 9, 10, 11). The partial peptide of Tojo is considered for the fragment of the FHOS protein of instant application (claim 12). Further Tojo teaches a cell such as yeast, animal cell etc. transformed by the DNA encoding the protein of the present invention capable of producing the protein of the present invention may also be used for the screening method of the present invention (claims 30, 31), see page 15, lines 3-8 of the reference. Therefore, claims 9-12, 27-31 of the instant application are being anticipated by Tojo et al.

This rejection was set forth in previous office action. In response Applicants traverse the rejection. The reason for the traversal is Tojo et al. does not teach each element of the claimed invention. Applicants arguments have been considered fully but not found persuasive because Tojo's protein II includes a human spleen derived protein containing the amino acid sequence of SEQ ID NO: 2, that is highly homologous (99.2%) to FHOS protein. Thus it is inherent. See the teaching of rest of the elements above. Thus 102 rejection as anticipated by Tojo remains.

Conclusions

Claims 9-12, 27-31, 45, 46 are rejected.

Claims 9-12, 27-46 are objected.

Inquiries

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is 571-272-0954. The examiner can normally be reached on M-F, 10:00 am-7:00 pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Rita Mitra, Ph.D.

July 20, 2006



ROBERT A. WAX
PRIMARY EXAMINER